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(54) Title: DISPERSION OF TASTE MASKED CRYSTALS OR GRANULES OF ACTIVE SUBSTANCES, CHEWABLE SOFT CAPSULES FILLED WITH SAID DISPERSION, AND PROCESS FOR PREPARING SAME

(57) Abstract: The present invention concerns a dispersion of crystals or granules of active substance in a lipophilic vehicle, said crystals or granules being coated by a coating for taste masking purposes. The invention also it concerns unit dosage forms and preferentially chewable or fast dissolving soft gelatin capsules filled with said dispersion as well as process for manufacturing same.

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AMENDED CLAIMS

[received by the International Bureau on 16 September 2004 (16.09.04);
Original claims 1-16 replace by new claims 1-16 unchanged; (4 pages).]

1. (iv) A dispersion of crystals or granules of active substance in a lipophilic vehicle, wherein said lipophilic vehicle has a solubilizing power for the active substance of less than 1.5 times the active substance concentration for which a taste is detected in water, and wherein said crystals or granules being coated by a coating for taste masking purposes.
3. (iv) The dispersion according to claim 1, wherein the lipophilic vehicle is selected from the group consisting of vegetable oils, animal oils, tri-, di- or mono-glycerides of fatty acids, lipolysing oils, mineral oils, light waxes, vaseline, silicone oil, simethicons, mixtures of silicone oil and colloidal silica, and mixtures thereof.
4. (i) The dispersion according to claim 1, wherein the lipophilic vehicle additionally comprises additives selected from the group consisting of sweeteners, flavorings, colorants, thickeners, dispersants, effervescent agents, super-disintegrants, lipophilic surfactants, hydrophilic surfactants, hydrosoluble agents and mixtures thereof.
5. (i) The dispersion according to claim 1, in which the concentration of active substance in the dispersion is at most 75% by weight in relation to the weight of the dispersion.
6. (i) The dispersion according to claim 1, wherein the coating of the crystals or granules of active substance is selected from ethylcellulose, hydroxyethylcellulose, hydroxypropylmethylcellulose,

hydroxypropylmethyl cellulose phthalate, methacrylic copolymer, lipidic compounds, lipophilic compounds, polyethylene glycol behenate, glycerol palmitostearate, glycerol stearate, cetyl palmitate, glyceric macrogol beeswaxes, glycerol, PEG-32 stearate, Peg-32 palmitostearate, and mixtures thereof.

7. (i) The dispersion according to claim 1, wherein the coating represents between 5 and 50% by weight of the total weight of the coated granules or crystals.
8. (i) The dispersion according to claim 1, wherein the average size of the coated crystals or granules is less than 300 μm .
9. (i) The dispersion according to claim 1, wherein the granules of active substances and/or the coating for taste masking purposes can comprise additives from the group consisting of colorants, sweeteners, flavorings, effervescent agents, super-disintegrants, lipophilic surfactants, hydrophilic surfactants, hydrosoluble agents and mixtures thereof.
10. (iv) The dispersion according to claim 1, wherein said lipophilic vehicle is a dimethicone, said coating being a mixture of ethyl cellulose and hydroxypropylmethylcellulose, said coating representing 5% to 70% of the total weight of the dispersion.
11. (iv) A chewable soft capsule comprising an outer envelope encapsulating the dispersion according to claim 1.
12. (iv) The soft capsule according to claim 1, in which the outer envelope

comprises gelatin, a plasticizer, and at least one starch, optionally amylum acetate.

13. (i) The soft capsule according to claim 12, in which the composition of said envelope also comprises an additive chosen from the group consisting of sweeteners, flavorings, colorants, and mixtures thereof.
14. (i) The soft capsule according to claim 11, wherein the outer envelope comprises between 18 and 30% by wt. gelatin, between 30 and 45% by wt. of plasticizer, between 3 and 12% by wt. of starch or amylum acetate and up to 12% by wt., of an unbleached starch and water to 100%, with these percentages being percentages by weight in relation to the total weight of said envelope composition.
15. (i) The soft capsule according to claim 14, in which the plasticizer is selected from the group consisting of polyols, glycerol, xylitol, sorbitol, polyglycerol, non-crystallisable solutions of sorbitol, glucose, fructose, glucose syrups, and mixtures thereof.
16. (iv) A process for preparation of chewable soft capsules, comprising the steps of:
 - a) preparing an outer envelope;
 - b) as necessary preparing granules of active substance;
 - c) coating the crystals of active substance or granules prepared above using a coating for taste masking purposes;
 - d) as necessary dispersing additives in a lipophilic vehicle, wherein said lipophilic vehicle has a solubilizing power for

the active substance of less than 1.5 times the active substance concentration for which a taste is detected in water, and optionally milling of this;

- e) dispersing the coated crystals or granules in the lipophilic vehicle;
- f) filling and sealing the capsules with said dispersion;
- g) drying the capsules.

Statement Under Article 19(1) (Rule 46.4)

The amendments to the claims have no impact on the description of the invention.

The amendments to claims 1 and 16 are primarily directed at incorporating previous claim 2 into independent claims 1 and 16.

The transmittal of the International Search Report occurred on August 27, 2004. Reference 1 was U.S. Patent No. 5,320,855. This patent is directed to specific coating formulations which provide for taste masked solid dosage forms/chewable tablets. This reference makes no suggestion nor discloses the use of a lipophilic vehicle that has a solubilizing power for the active substance of less than 1.5 times the active substance concentration for which a taste is detected in water.

D2, U.S. Patent No. 4,851,226, is similar to D1 and fails to disclose the use of a lipophilic vehicle for a dispersion of crystals or granules of an active substance that has been coated for taste-masking purposes.

D3, U.S. Patent No. 5,019,563 is directed to a taste masking of ibuprofen through the use of β -cyclodextrin complexation. This patent does not refer to the development of coated particles and therefore does not come under the scope of the claims.